Enclosure No:	**1/AWMSG/0717**
Agenda Item No:	**1** – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Minutes of the AWMSG meeting held Wednesday, 21st June 2017 commencing 9.30 am in the Park Inn Hotel, Cardiff North, Circle Way East, Llanedeyrn, Cardiff, CF23 9XF

VOTING MEMBERS PRESENT:

			Did not participate in
1.	Dr Stuart Linton	Chair & Hospital Consultant	
2.	Dr Cath Bale	Hospital Consultant	
3.	Dr Anwen Cope	Healthcare professional eligible to prescribe	
4.	Mr Stuart Davies	Finance Director	
5.	Mr Stefan Fec	Community Pharmacist	
6.	Prof Dyfrig Hughes	Health Economist	
7.	Mrs Mandy James	Senior Nurse	
8.	Dr Emma Mason	Clinical Pharmacologist	
9.	Mrs Susan Murphy	Managed Sector Primary Care Pharmacist	
10.	Mr Rob Thomas	ABPI Cymru Wales	
11.	Mr Chris Palmer	Lay Member	
12.	Mr Roger Williams	Managed Sector Secondary Care Pharmacist	
13.	Dr Jeremy Black	General Practitioner	
14.	Dr Mark Walker	Medical Director	
15.	Professor John Watkins	Public Health Wales	

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair
Dr Robert Bracchi, CAPIG Chair
Mrs Karen Samuels, Head of PAMS, AWTTC
Mr Anthony Williams, Senior Pharmacist & Team Leader, AWTTC

Dr David Jarrom Senior Scientist, AWTTC
Mrs Sabrina Rind, Senior Pharmacist, AWTTC
Mr Richard Boldero, Senior Pharmacist, AWTTC
Mrs Claire Thomas, Senior Pharmacist, AWTTC

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
ASAR	AWMSG Secretariat Assessment Report
AWMSG	All Wales Medicines Strategy Group
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
BMA	British Medical Association
CAPIG	Clinical and Patient Involvement Group
CEPP	Clinical Effectiveness Prescribing Programme
CHMP	Committee for Medicinal Products for Human Use
DoH	Department of Health
ECDF	English Cancer Drugs Fund
EMA	European Medicines Agency
EMIG	Ethical Medicines Industry Group
EOL	End of life
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
HST	Highly Specialised Technology
HTA	Health Technology Appraisal
IR	Independent Review
MHRA	Medicines and Healthcare products Regulatory Agency
MMPB	Medicines Management Programme Board
M&TCs	Medicines & Therapeutics Committees
NICE	National Institute for Health and Care Excellence
NMG	New Medicines Group
PAMS	Patient Access to Medicines Service
PAR	Preliminary Appraisal Recommendation
PAS	Patient Access Scheme
PPRS	Prescription Price Regulation Scheme
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
UHB	University Health Board
WAPSU	Welsh Analytical Prescribing Support Unit
WCPPE	Welsh Centre for Pharmacy Postgraduate Education
WeMeReC	Welsh Medicines Resource Centre
WG	Welsh Government
WHO	World Health Organization
WHSSC	Welsh Health Specialised Services Committee
WPAS	Wales Patient Access Scheme

1. Welcome and introduction

The Chairman opened the meeting and welcomed members.

2. Apologies

Dr Sian Lewis, Welsh Health Specialised Services Committee
Dr Pushpinder Mangat, Welsh Health Specialised Services Committee

3. Declarations of interest

Members were reminded to declare any interests. There were none.

4. Minutes of previous meeting

The draft minutes of the previous meeting were checked for accuracy and approved.

5. Appraisal 1: Full Submission (WPAS)

Ivacaftor (Kalydeco) for the treatment of patients with cystic fibrosis (CF) aged 18 years and older who have an *R117H* mutation in the CFTR gene

The Chairman welcomed delegates from Vertex Pharmaecuticals.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared. The Chairman explained that all individuals remaining in the public gallery were associated with AWTTC and the company delegates confirmed they were happy to proceed with the appraisal.

The Chairman explained that AWMSG had appraised ivacaftor (Kalydeco) in March 2017 for patients with the *R117H* mutation in the CFTR gene and recommended that the medicine should not be recommended as the case for cost-effectiveness had not been proven. Subsequent to the meeting, the company had requested an independent review as there was no opportunity for a CAPIG meeting to be held to consider in more detail any additional issues from the clinical and patient perspective prior to appraisal by AWMSG. The Chairman confirmed that he had agreed that a CAPIG meeting be convened and that AWMSG should reappraise the medicine and take into account the outcome of the CAPIG meeting.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on health boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman explained that NMG had considered the clinical and cost effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation and the report from the CAPIG group. He explained that members would focus on the budget impact and wider societal issues.

The Chairman confirmed that AWMSG's policy for appraising medicines for orphan, ultra-orphan medicines and medicines developed specifically for rare diseases had been tabled.

Sabrina Rind, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. Members were made aware that the medicine had not been routinely recommended for this indication by the SMC in Scotland. It was confirmed that WHSSC were not aware that the medicine for this indication is being commissioned in NHS England. It was noted that the effect size of ivacaftor treatment in this population with *R117H* mutation was smaller than that seen in other mutation types such as *G551D* but that ivacaftor significantly improved lung function above the minimal clinically important difference. It was outlined that this is the first medicine for CF which targets the underlying gene defect.

Dr. Robert Bracchi updated members on the CAPIG meeting which was convened. Members were informed that clinicians had developed All Wales criteria to identify those patients with the *R117H* mutation who should be treated within Wales. CAPIG had been provided with patient stories detailing how the medicine had transformed the lives of patients with a *G551D* mutation and clinicians advised there are currently three patients with the *R117H* mutation who are being considered for addition to the lung transplant list. Patients had outlined in the CAPIG meeting the significant burden of the condition and the impact on their daily life. Dr Bracchi highlighted that clinicians and patients reported that a negative recommendation by AWMSG would create an inequity in the treatment of patients with CF living in Wales.

Dr Al-Ismail confirmed that NMG had appraised ivacaftor (Kalydeco) on 8th February 2017 and recommended its use within NHS Wales for the treatment of patients with CF aged 18 years and older who have an *R117H* mutation in the CFTR conductance regulator (*CFTR*) gene. The view of NMG was that the recommendation should apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

Dr Al-Ismail confirmed that NMG considered ivacaftor satisfied the AWMSG criteria for ultra-orphan status.

Mrs Rind relayed the views of clinical experts. She highlighted that clinical experts noted the potential ivacaftor has to transform the disease process and highlighted the importance of starting therapy in early disease. Experts highlighted that there is evidence to suggest that patients with the *R117H* mutation become symptomatic at an older age but decline at the same rate as patients with more severe mutations. Mrs Rind informed members that clinical experts have provided an All Wales consensus statement agreeing the criteria that would identify patients suitable to be treated with ivacaftor and agreed a proposed algorithm for treatment. The role of FEV1 in the monitoring of treatment was discussed and the company clarified that this outcome would be monitored during treatment. The monitoring parameters in the current WHSSC clinical access policy for the existing use of Ivacaftor in Wales were highlighted to members.

The effect size of ivacaftor for the *R117H* mutation compared to *G551D* was discussed and it was noted that the cost per QALY was significantly higher for this mutation than for the *G551D* mutation. The company noted that although the effect is smaller in *R117H*, it is still a clinically significant effect. Members asked about the availability of longer term data and improved survival data and the company advised that longer term data are being collected and they have registry data which is showing real life benefits for patients.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness and highlighted the limitations of the submission. The Chairman reminded members of the latitude applied in appraising an orphan and ultra-orphan medicine, and medicines developed specifically for rare diseases. Members noted that the ICER was extremely high and noted the opportunity cost involved in approving this medicine.

The discussion moved on to the budget impact and the Chairman asked members to consider the budget impact estimates in the ASAR. It was noted that clinical experts have advised that the expected numbers of eligible patients will half the budget impact estimated by the company.

The Chairman confirmed that several patient organisation questionnaires had been received and, for the purposes of transparency, asked Mr Chris Palmer to relay the key issues highlighted in the submissions. Mr Palmer relayed the strong patient support for this medicine. It offers patients an opportunity to plan ahead and be involved in everyday life, and to have a

better quality of life.

The Chairman asked members to highlight any wider societal issues. It was noted that patients with the *R117H* gene are generally older and that some patients have young children. It was stated that the disease also impacts on a patient's ability to work. It was highlighted that there may be equity considerations if this indication received a negative recommendation as patients with severe disease may be unable to access treatment when the medicine has already been approved for patients in Wales with other mutations.

Having confirmed that there were no outstanding issues, the Chairman asked the delegates for their closing remarks. Confirmation was received that the appraisal process had been fair and transparent and that all relevant issues had been discussed. The Chairman closed the appraisal and members retired to vote in private.

The meeting re-convened and the Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Ivacaftor (Kalydeco) is recommended for restricted use within NHS Wales for the treatment of patients with cystic fibrosis (CF) aged 18 years and older who have an *R117H* mutation in the CF transmembrane conductance regulator (*CFTR*) gene.

This recommendation will apply only when people are treated in line with the relevant Welsh clinical access policy.

This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days to the applicant company who have up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

6. Chairman's Report (verbal update)

The Chairman informed members that a second article on AWMSG's Citizen's Jury had been published in Welsh Pharmacy Review. The next article will focus on medicines safety and will highlight best prescribing practice in line with AWMSG's 15 year conference which will be held in Cardiff on the 27th and 28th June.

The Chairman reported that Welsh Government ratification of AWMSG's advice in relation to bevacizumab (Avastin), vismodegib (Erivedge) and emtricitabine/tenofovir disoproxil fumarate (Truvada) remains outstanding. The manufacturer and the service would be informed when ratification is received.

The Chairman confirmed that in the absence of a submission, the following medicines cannot be endorsed for use within NHS Wales:

Alectinib (Alecensa) [AWTTC ref: 2385] as monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer previously treated with crizotinib.

Botulinum A toxin (Dysport) [AWTTC ref: 2638] as a symptomatic treatment of focal spasticity of lower limbs in adults affecting the ankle joint due to stroke or traumatic brain injury (TBI).

Canakinumab (Ilaris) [AWTTC ref: 2093] for the treatment of tumour necrosis factor (TNF)

receptor associated periodic syndrome (TRAPS) in adults, adolescents and children aged 2 years and older; treatment of hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD) in adults, adolescents and children aged 2 years and older; treatment of Familial Mediterranean Fever (FMF) in adults, adolescents and children aged 2 years and older. Ilaris should be given in combination with colchicine, if appropriate.

Fludrocortisone acetate [AWTTC ref: 3482] as partial replacement therapy for primary and secondary adrenocortical insufficiency in Addison's disease and for the treatment of salt-losing adrenogenital syndrome.

Human normal immunoglobulin (Cuvitru) [AWTTC ref: 3338] as a replacement therapy in adults, and children and adolescents (0-18 years) in:
Primary immunodeficiency syndromes with impaired antibody production; Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (CLL), in whom prophylactic antibiotics have failed or are contra-indicated; Hypogammaglobulinaemia and recurrent bacterial infections in multiple myeloma (MM) patients; Hypogammaglobulinaemia in patients pre- and post-allogeneic haematopoietic stem cell transplantation (HSCT)

Lenalidomide (Revlimid) [AWTTC ref: 810] as monotherapy for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.

lixisenatide/insulin glargine (Suliqua) [AWTTC ref: 2464] for use in combination with metformin for the treatment of adults with type-2 diabetes mellitus to improve glycaemic control when this has not been provided by metformin alone or metformin combined with another oral glucose lowering medicinal product or with basal insulin.

Mercaptamine (Cystadrops) [AWTTC ref: 3316] for the treatment of corneal cystine crystal deposits in adults and children from 2 years of age with cystinosis.

The Chairman informed the committee that the NICE HST Final Evaluation Determination had been issued in relation to eligustat for the long-term treatment of adult patients with Gaucher disease type 1. At the AWMSG Steering Committee held on 6th June, Welsh Health Specialised Services Committee confirmed that there were no barriers to the implementation of this advice within NHS Wales. The Chairman confirmed AWMSG's recommendation to the Cabinet Secretary would be to accept NICE HST advice for eligustat.

The Chairman announced the appraisals scheduled for the next meeting on 19th July 2017 in Cardiff:

Appraisal 1: Full Submission
Desmopressin acetate (Noqdirna) for the treatment of symptomatic nocturia due to idiopathic nocturnal polyuria in adults
Applicant Company: Ferring Pharmaceuticals (UK)

Appraisal 2: Limited Submission (WPAS)
Adalimumab (Humira) for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adolescents from 12 years of age with an inadequate response to conventional systemic therapy
Applicant Company: AbbVie Ltd

Appraisal 3: Limited Submission
Cefuroxime (Aprokam) for use as antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery.
Applicant Company: Thea Pharmaceuticals Ltd

Appraisal 4: Limited Submission
Triamcinolone hexacetonide for the treatment of juvenile idiopathic arthritis
Applicant Company: Intrapharm Laboratories Ltd

Members were reminded to declare any interests in relation to these appraisals before the next meeting. Patients, patient organisations and patient carers were invited to submit their views on the medicines scheduled for appraisal.

7. National Prescribing Indicators 2016–2017: Analysis of Prescribing Data to Dec 2016

Mrs Claire Thomas and Mr Richard Boldero presented an analysis of the National Prescribing Indicators (NPIs), for the third quarter of 2016–2017, to AWMSG for information. For the current year, 13 primary care NPIs focus on seven therapeutic areas and the reporting of adverse reactions to medicines via the Yellow Card Scheme, in addition to three NPIs for secondary care. Mrs Thomas highlighted that there had been improvements across Wales, in line with the aims of the indicators, for 11 of the 12 primary care NPIs with a threshold, compared with the equivalent quarter of the previous year. The indicator which did not show an improvement was gabapentin and pregabalin prescribing, which had increased by 9.73%. The NPIs associated with the greatest improvements were Yellow Card reporting by GPs, which demonstrated a 39% increase, and co-amoxiclav, cephalosporins and NSAIDs which all demonstrated reductions.

Mr Boldero presented the analysis for the secondary care NPIs. The antibiotic surgical prophylaxis indicator value reduced by 2% in comparison to the previous quarter of 2016–2017. For the insulin prescribing and prescribing of biosimilars NPIs the quarter for comparison was the equivalent quarter of 2015–2016. In primary care and secondary care there were decreases of 0.08% and 5.75% in the use of long-acting insulin analogues respectively. For the prescribing of biosimilars NPI there was an increase in the use of the filgrastim biosimilars from 97.9% to 98.7%, for infliximab biosimilar use there was an increase from 19% to 53%, and for insulin glargine biosimilar an increase from 0.02% to 1.84%. All of these changes are in keeping with the aim of the NPI.

The Chairman opened discussion and there was debate around several of the NPIs. For the biosimilar indicator, NPI members asked whether newly licensed biosimilars would be included in future reports. Mr Boldero confirmed that etanercept and rituximab would be provided in the quarterly analysis of the 2017–2018 NPIs. Several members also suggested that further intelligence around the use of biosimilars be provided; it was agreed that this would be considered. Mrs Samuels suggested that the best practice day being held on the 28th June 2017 will be a very good opportunity to allow sharing across health boards in Wales.

8. All Wales multidisciplinary medicines reconciliation policy

Mr Roger Williams presented the all Wales multidisciplinary medicines reconciliation policy. This policy document has been developed to provide healthcare professionals with information to promote the safe and timely completion of medicines reconciliation for patients moving between care settings. Explanation to the background of the policy was provided including the joint NPSA/NICE alert from 2007 as well as the Welsh Government Patient Safety Notice from 2016. Members were also reminded of the report issued by HM Coroner in 2016 where concerns were raised that there may be health boards/trusts in Wales without a medicines reconciliation policy in place. The benefits of a single policy for use in Wales were highlighted.

Mr Williams informed members that this policy has been developed by the all Wales Chief Pharmacists, Quality and Patient Safety Group and has been out to consultation. Members were requested to consider the policy for endorsement and the Chair asked for any comments.

Discussion was held around some aspects of the policy, particularly in relation to timescales for the transfer of patient information and the wider supporting processes, including appropriate

training and awareness raising. It was agreed that some minor changes could be made with some additional wording. The Chair closed the discussion confirming members' strong support for the policy and its endorsement.

9. Appraisal 2: Full Submission

Aviptadil phentolamine (Invicorp) for symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasulogenic, psychogenic, or mixed aetiology

The Chairman welcomed delegates from Evolan Pharma AB.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on health boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman explained that NMG had considered the clinical and cost effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

Dr David Jarrom, AWTTC appraisal lead, set the context of the appraisal and highlighted the key aspects of the submission outlined in the ASAR. He highlighted that this is a resubmission with an updated and more comprehensive health economic model included. It was stated that the company have proposed a restricted recommendation for use in people with erectile dysfunction that has not responded to oral therapy. The views of clinical experts were relayed and it was confirmed that their views of the anticipated place in therapy reflected that proposed by the company, and that this group of patients had few other treatment options available.

Dr Al-Ismail confirmed that an appraisal by the NMG had been undertaken on 3rd May 2017. He relayed NMG's recommendation to AWMSG that aviptadil phentolamine (Invicorp) should not be recommended for use within NHS Wales for the symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasulogenic, or mixed aetiology. It was the view of NMG that the clinical and cost-effectiveness data presented in the submission were insufficient to recommend its use. There were concerns with the justification of inclusion of a cost-minimisation model and that the clinical evidence submitted was not specific to the restricted subpopulation.

The Chairman opened the discussion on clinical effectiveness. Issues in the company response to the PAR that aim to address the limitations in the clinical evidence were discussed. It was acknowledged that some aspects of the design of the trial introduced the possibility of bias, but that the nature of the condition made this unavoidable, and that any bias was likely to be in favour of the comparator. It was also noted that the trial population did not specifically include people with erectile dysfunction that had not responded to oral PDE5i therapy, because these treatments were not available at the time the trial was carried out. It was highlighted that there had been significant shortages of the comparator in the last 12-18 months and that without aviptadil phentolamine there would be no other treatment options.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness and the budget impact. Professor Hughes confirmed that he took no part in the production of the ASAR

and was in attendance as the voting health economist member of AWMSG. It was noted that a cost-minimisation analysis was submitted, which predicts some small cost savings from the use of aviptadil phentolamine compared to the comparator treatment, Caverject. However, there was some uncertainty over whether aviptadil phentolamine and Caverject were equivalent. It was noted that the two treatments have the same cost at the doses used in the model, but that Caverject is available as a range of other doses and preparations. It was confirmed that aprostadil injection is currently the most widely used preparation, and that whilst other alprostadil doses were sometimes used, these were higher doses and therefore more costly than Aviptadil phentolamine.

It was noted that a range of scenario analyses were included, some provided by the company and some conducted by AWTTC, to explore the effect of different numbers of consultant visits and inclusion of adverse events. In all scenarios aviptadil phentolamine remained the cost saving option.

Details of the budget impact were provided by Professor Hughes. The company confirmed that there were associated savings in year two and beyond.

The Chairman confirmed that a patient organisation questionnaire had been received from The Sexual Advice Association, and for the purposes of transparency, asked Mr Chris Palmer to relay the key issues highlighted in the submission. It was relayed that aviptadil phentolamine was felt to be an effective second line therapy when caverject is too painful to administer.

In concluding, the Chairman thanked the company delegates and, having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal. Members retired to vote in private.

Appraisal decision subsequently announced in public:
The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Aviptadil/phentolamine (Invicorp) is recommended as an option for the symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasculogenic, psychogenic, or mixed aetiology.

Aviptadil/phentolamine (Invicorp) is restricted to use in people with erectile dysfunction that has not responded to oral PDE5 inhibitor therapy.

Aviptadil/phentolamine (Invicorp) is not recommended for use within NHS Wales outside of this subpopulation.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days to the applicant company who have up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

The Chairman closed proceedings

Date of next meeting – Wednesday, 19th July 2017 in Cardiff